REMARKS

Claims 1 - 7 and 22 - 50 are pending in the above-identified application. Claims 6, 22 - 26, 28 - 30, 33 - 36 and 38 - 50 are withdrawn from consideration.

In the Office Action of July 16, 2003, Claims 2, 7, 27, 31, 32 and 37 were rejected. Claim 1 was objected to. Claims 3 - 5 were allowed. In response, Claims 2 and 5 are canceled, and Claims 1, 7, 27 and 37 are amended. Reexamination and reconsideration are respectfully requested in view of the foregoing amendments and the following remarks.

Objections to the Specification

The specification was objected to on the alleged grounds that it contains the recitation of amino acid sequences without reference to a sequence identifier (page 5, line 16 and 18, and Claim 2).

In response, the specification is amended to designate the sequence Asp-Ser-Gly-Xaa-Xaa-Ser as SEQ ID NO:9. A revised sequence listing containing SEQ ID NO:9 is included with this response, along with a revised computer-readable copy of the sequence listing.

Accordingly, it is respectfully submitted that this objection is overcome.

The specification is further amended to correct minor typographical errors. It is respectfully submitted that the errors would be obvious to persons skilled in the art and that no new matter is introduced into the specification.

Objections to the Claims

Claim 1 was objected to on the alleged grounds that the sequence identifier should be identified as "SEQ ID NO:2" rather than "SEQ ID No. 2". In response, Claim 1 is amended accordingly.

Claims 7, 31 and 32 were objected to on the alleged grounds that they encompass polynucleotides encoding peptides devoid of the F box and peptides devoid of WD units and therefore encompass non-elected subject matter. In response, Claim 7 is amended to be directed to a nucleic acid coding for the protein h-βTrCP. Accordingly, amended Claim 7, and Claims 31 and 32, which depend from Claim 7, do not encompass polynucleotides encoding peptides devoid of the F box and peptides devoid of WD units

Accordingly, it is respectfully submitted that the objections to the claims are thereby overcome.

Rejection of Claims 2, 5, 27, 37 under 35 U.S.C. §112, second paragraph

Claims 2, 5, 27 and 37 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

Regarding Claim 2, the Examiner alleges that the phrase "especially" renders the claim indefinite. This rejection is moot because Claim 2 is canceled herein. The limitations of Claim 2 are incorporated into amended Claim 1, but the term "especially" is not used in the amended Claim 1.

Regarding Claim 5, the Examiner alleges that the claim is unclear as to what sequence the amino acid positions listed in the claim refer. This rejection is moot because Claim 5 is canceled herein. The limitations of Claim 5 are incorporated into

amended Claim 1, wherein it is clear that the amino acid positions listed in the claim refer to SEQ ID NO:2.

Regarding Claim 27, the Examiner alleges that the claim is indefinite because it is drawn to peptide fragments of Claim 7 whereas Claim 7 is drawn to nucleic acid sequences and that it is unclear what is meant by "which have conserved both the WD units and the F-box. Claim 27 is amended herein to depend from Claim 6, which is a non-elected claim. Accordingly, Claim 27 should be treated as withdrawn from further consideration as a non-elected claim.

Regarding Claim 37, the Examiner alleges that the nexus between the capability of the anti-HIV antiviral agent candidates to inhibit the interaction between human β-TrCP protein and Vpu protein and identifying the candidate as an anti-HIV-1 antiviral agent. The Examiner alleges that the goal of the method ("identifying anti-HIV-1 antiviral agents") appears to be different from that of the endpoint (determining "the capability of the anti-HIV antiviral agent candidates to inhibit the interaction between h-βTrCP protein and Vpu protein"). Thus, the Examiner alleges that the claim is unclear as to which of the candidates that inhibit the interaction between h-βTrCP protein and Vpu protein is considered an anti-HIV-1 antiviral agent and is unclear as to how the h-βTrCP protein is used in screening.

The rejection of Claim 37 under 35 U.S.C. §112, second paragraph, is respectfully traversed. The method of Claim 37 is a method for identifying anti HIV-1 antiviral agents in which the identification is made by determining the capacity of the anti-HIV-1 antiviral agents to inhibit the interaction between h- βTrCP and Vpu protein. Claim 37 is amended for clarification that the candidates that inhibit the interaction between h-βTrCP and Vpu protein are considered as anti HIV-1 antiviral agents. The

screening step is the screening for inhibition of h- βTrCP binding to Vpu. Accordingly, it is respectfully submitted that amended Claim 37 is not unclear or indefinite.

Accordingly, it is respectfully submitted that the rejections of Claims 2, 5 and 37 under 35 U.S.C. §112, second paragraph, are thereby overcome.

Rejection of Claims 7, 27, 31, 32 and 37 under 35 U.S.C. §112, first paragraph

Claims 7, 27, 31, 32 and 37 were rejected under 35 U.S.C. §112, first paragraph, on the alleged grounds that the specification does not provide enablement for 1) a nucleic acid sequence coding for a peptide fragment that results from addition, deletion and/or replacement of one or more amino acids of a β-TrCP protein characterized in that is consists of (a) a DNA sequence of the nucleic acid fragment coding for said peptide fragment or (b) a DNA sequence that hybridizes with the above sequence or one of its fragments or (c) a DNA sequence which results from the sequences (a) or (b) and codes for the human β-TrCP fragments, 2) expression vectors or host cells containing the nucleic acid sequences or 3) antitumoral agent which consist of the peptide fragments.

In response, Claims 7 and 37 are amended to delete limitations relating to peptide fragments. (Claim 27 is amended to depend from a non-elected claim and therefore should be treated as withdrawn from consideration.) Claims 31 and 32 depend from the amended Claim 7. Accordingly, it is respectfully submitted that Claims 7, 31, 32 and 37 as amended relate to polynucleotides for which the specification provides enablement.

Accordingly, it is respectfully submitted that the rejection of Claims 7, 27, 31, 32 and 37 under 35 U.S.C. §112, first paragraph, for alleged lack of enablement is thereby overcome.

Rejection of Claims 7, 27, 31 and 32 under 35 U.S.C. §112, first paragraph

Claims 7, 27, 31 and 32 were rejected under 35 U.S.C. §112, first paragraph, on the alleged grounds that the specification contains subject matter that is not described in the specification. In particular, the Examiner alleges that the claims are drawn to a genus of nucleic acid sequences coding for a peptide fragment of human b-trCP having any number of amino acid additions, deletions, and/or replacements.

In response, Claim 7 is amended to delete limitations relating to peptide fragments. (Claim 27 is amended to depend from a non-elected claim and therefore should be treated as withdrawn from consideration.) Claims 31 and 32 depend from the amended Claim 7. Accordingly, it is respectfully submitted that Claims 7, 31 and 32 as amended relate to polynucleotides for which the specification provides a written description.

Accordingly, it is respectfully submitted that the rejection of Claims 7, 27, 31 and 32 under 35 U.S.C. §112, first paragraph, for alleged lack of written description is thereby overcome.

Rejection of Claims 7, 31 and 32 under 35 U.S.C. §102(a) over Skowyra et al

Claims 7, 31 and 32 are rejected under 35 U.S.C. §102(a) as anticipated by Skowyra et al. (Cell (1997)91: 209-219). The Examiner alleges that Skowyra discloses nucleic acid sequences coding for peptide fragments that result from addition, deletion and/or replacement of one or more amino acids of the b-TrCP protein.

In response, Claim 7 is amended to delete limitations relating to peptide fragments. Claims 31 and 32 depend from the amended Claim 7. As indicated by the Examiner on page 15 of the outstanding Office Action, the prior art does not reveal any teachings or suggestions of H-βTrCP, the protein of the present invention. Skowyra

therefore does not teach or suggest any nucleic acid coding for the human protein h-βTrCP. Accordingly, it is respectfully submitted that Claims 7, 31 and 32 as amended are limited to polynucleotides that are not anticipated by Skowyra.

Accordingly, it is respectfully submitted that the rejection of Claims 7, 31 and 32 under 35 U.S.C. §102(a) over Skowyra is thereby overcome.

Rejection of Claims 7, 31 and 32 under 35 U.S.C. §102(b) over Bour et al

Claims 7, 31 and 32 are rejected under 35 U.S.C. §102(b) as anticipated by Bour et al (J. Virol. (1995)69(3): 1510-1520)). The Examiner alleges that Bour discloses nucleic acid sequences coding for peptide fragments that result from addition, deletion and/or replacement of one or more amino acids of the b-TrCP protein.

In response, Claim 7 is amended to delete limitations relating to peptide fragments. Claims 31 and 32 depend from the amended Claim 7. As indicated by the Examiner on page 15 of the outstanding Office Action, the prior art does not reveal any teachings or suggestions of H-βTrCP, the protein of the present invention. Bour therefore does not teach or suggest any nucleic acid coding for the human protein h-βTrCP. Accordingly, it is respectfully submitted that Claims 7, 31 and 32 as amended are limited to polynucleotides that are not anticipated by Bour.

Accordingly, it is respectfully submitted that the rejection of Claims 7, 31 and 32 under 35 U.S.C. §102(b) over Bour is thereby overcome.

Rejection of Claims 7, 31 and 32 under 35 U.S.C. §102(b) over Rubinfeld et al

Claims 7, 31 and 32 are rejected under 35 U.S.C. §102(b) as anticipated by Rubinfeld (J. Biol. Chem (1995) 270(10): 5549-5555). The Examiner alleges that Rubinfeld discloses nucleic acid sequences coding for peptide fragments that result

from addition, deletion and/or replacement of one or more amino acids of the β-TrCP protein.

In response, Claim 7 is amended to delete limitations relating to peptide fragments. Claims 31 and 32 depend from the amended Claim 7. As indicated by the Examiner on page 15 of the outstanding Office Action, the prior art does not reveal any teachings or suggestions of H-βTrCP, the protein of the present invention. Rubinfeld therefore does not teach or suggest any nucleic acid coding for the human protein h-βTrCP. Accordingly, it is respectfully submitted that Claims 7, 31 and 32 as amended are limited to polynucleotides that are not anticipated by Rubinfeld.

Accordingly, it is respectfully submitted that the rejection of Claims 7, 31 and 32 under 35 U.S.C. §102(b) over Rubinfeld is thereby overcome.

Rejection of Claims 7 and 31 under 35 U.S.C. §102(b) over Inoue et al

Claims 7 and 31 are rejected under 35 U.S.C. §102(b) as anticipated by Inoue (Proc. Natl. Acad. Sci. (1992) 89 4333-4337)). The Examiner alleges that Inoue discloses nucleic acid sequences coding for peptide fragments that result from addition, deletion and/or replacement of one or more amino acids of the b-TrCP protein.

In response, Claim 7 is amended to delete limitations relating to peptide fragments. Claim 31 depends from the amended Claim 7. As indicated by the Examiner on page 15 of the outstanding Office Action, the prior art does not reveal any teachings or suggestions of H-βTrCP, the protein of the present invention. Inoue therefore does not teach or suggest any nucleic acid coding for the human protein h-βTrCP. Accordingly, it is respectfully submitted that Claims 7 and 31 as amended are limited to polynucleotides that are not anticipated by Inoue.

Accordingly, it is respectfully submitted that the rejection of Claims 7 and 31 under 35 U.S.C. §102(b) over Inoue is thereby overcome.

Conclusion

In view of the foregoing amendments and remarks, it is respectfully submitted that Claims 1, 3, 4, 7, 31, 32 and 37 are in condition for allowance. Favorable reconsideration is respectfully requested.

Should the Examiner believe that anything further is necessary to place this application in condition for allowance, the Examiner is requested to contact applicants' undersigned attorney at the telephone number listed below.

Kindly charge any additional fees due, or credit overpayment of fees, to Deposit Account No. 01-2135 (935.38812X00).

Respectfully submitted,

ANTONELLI, TERRY, STOUT & KRAUS, LLP

By _____
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Attachment: Marked-Up Copy To Show Changes Made

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ATTACHMENT

MARKED-UP COPY TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Please replace the paragraphs from page 5, line 13 to page 5, line 25 with the following:

Via its WD units, the h-βTrCp protein of the invention is capable of interacting with proteins degradable by proteasome, particularly with virus proteins and cell proteins which possess the phosphorylation unit comprising the amino acids Asp-Ser-Gly-Xaa-Xaa-Ser (SEQ ID NO: 9), in which Xaa is any natural amino acid and in which the serine residues are phosphorylated.

The phosphorylation of this unit Asp-Ser-Gly-Xaa-Xaa-Ser (SEQ ID NO: 9) is essential to the ubiquitinylation and subsequent degradation of proteins possessing this type of unit. The h-βTrCP protein is only capable of interacting with proteins containing this unit when the two serine residues are phosphorylated, and it cannot interact with proteins containing a phosphorylation unit in which the serine residues are mutated to non-phosphorylatable amino acids. By interacting with the phosphorylated proteins on this unit, the h-βTrCP protein controls their ubiquitinylation and their screening towards degradation by proteasome.

Please replace the paragraph beginning on page 20, line 4, with the following new paragraph:

The cDNA of the h-βTrCP protein of SEQ ID No. 1 was amplified by carrying out PCR on 2 µg of plasmid DNA from the pGAD cDNA library using two amplification turns,

the outer pair of primers for the first turn consisting of the sense primer A of SEQ ID No. 3 (in pGAD1318) and the antisense primer B of SEQ ID NO. 4 (in ~~VPB1~~ VBP1) and the inner pair of primers for the second turn consisting of the sense primer C of SEQ ID No. 5 (in pGAD 1318) and the antisense primer D of SEQ ID No. 6 (in ~~VPB1~~ VBP1).

IN THE CLAIMS:

1. (amended) Human βTrCP protein (h- βTrCP) for the targeting of proteins towards proteasome degradation pathways, ~~characterized in that it has SEQ ID No. 2~~ said protein being capable of interacting with proteins degradable by proteasome, which possess the phosphorylation unit comprising the amino acids Asp-Ser-Glu-Xaa-Xaa-Ser (SEQ ID NO:9), in which Xaa is any natural amino acid and the serine residues are phosphorylated and said protein comprising the following units having the following positions in the sequence SEQ ID NO:2:

-F-box: amino acids 147 - 191,

-first WD unit: amino acids 259 - 292,

-second WD unit: amino acids 304 - 332,

-third WD unit: amino acids 343 - 373,

-fourth WD unit: amino acids 387 - 415,

-fifth WD unit: amino acids 427 - 455,

-sixth WD unit: amino acids 467 - 492, and

-seventh WD unit: amino acids 516 - 544.

7. (twice amemded) A nucleic acid sequence coding for the human protein ~~h-bTrcp~~ h-βTrCP according to Claim 1 ~~or a peptide fragment that results from the addition, deletion and/or replacement of one or more amino acids, said peptide~~

~~fragment having conserved the activity of interacting with the Vpu protein of HIV-1, the cell protein IκB or the cell protein β-catenin and/or with the skp1p protein~~, characterized in that it consists of:

a) the DNA sequence SEQ ID No. 1 ~~or a DNA sequence of the nucleic acid fragment coding for said peptide fragment~~;

b) a DNA sequence which hybridizes under strict conditions with the above sequence ~~or one of its fragments~~;

c) A DNA sequence which, due to the degeneracy of the genetic code, results from the sequences a) and b) above and codes for the human protein h-βTrCP ~~or fragments thereof~~; or

d) a mRNA and cDNA sequence corresponding to a), b), or c).

27. (amended) Antitumoral agents which consist of the peptide fragments of the h-βTrCP protein according to claim ~~7~~ 6 and which have conserved both the WD units and the F-box.

37. (amended) A method of identifying anti-HIV-1 antiviral agents, the method comprising the step of screening anti-HIV antiviral agent candidates using the h-βTrCP protein of Claim 1~~, or a fragment thereof,~~ to determine the capability of the anti-HIV antiviral agent candidates to inhibit the interaction between h-βTrCP protein and Vpu protein, wherein an anti-HIV antiviral agent candidate that inhibits binding between h-βTrCP protein and Vpu protein is identified as an anti-HIV-1 antiviral agent.